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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/615,703	07/09/2003	Stephen J. Benkovic	00-387-P	5892

20306 7590 06/18/2007
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EXAMINER

WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
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1639

MAIL DATE	DELIVERY MODE
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06/18/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/615,703

Applicant(s)

BENKOVIC ET AL.

Examiner

T. D. Wessendorf

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,7-16 and 18-44 is/are pending in the application.
- 4a) Of the above claim(s) 4,7,8,15,18,19,23-40 and 43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5,9-14,16,20-22,41,42 and 44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims Status

Claims 1-5, 7-16 and 18-44 are pending.

Claims 4, 7-8, 15, 18-19, 23-40 and 43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species.

Claims 1-3, 5, 9-14, 16, 20-22, 41-42 and 44 are under consideration.

Priority

This instant application is a CIP of three applications, which are 09/996,420 filed 11/29/2001, 09/578,991 filed 05/25/2000, and 09/296,137 filed 03/16/1999. 09/578,991 claims benefit to three provisional applications, which are 60/135,870 filed 05/25/1999, 60/154,582 filed 09/17/1999, and 60/174,256 filed 01/03/2000. 09/296,137 is a 371 of PCT/US97/16,593 filed 09/17/1997, which claims benefit to 60/020,089 filed 09/19/1996. However, only the limitations of 'A method for treating an animal against a microbe-induced disease' of claims 1-3, 5, 9-14, 16, 20, 21, 22, 41, 42, and 44 are granted the benefit of priority under 35 U.S.C. 120 for 09/996,420 and 09/578,991, because the limitations of 'A method for treating an animal against a microbe-induced disease' are directed to subject matter not adequately disclosed under 35 USC

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112, first paragraph, in either the parent application, i.e. 09/296,137, nor the PCT international application, i.e. PCT/US97/16,593. In a continuation-in-part application, only claims directed solely to subject matter adequately disclosed under 35 USC 112, first paragraph in the parent application is entitled to the benefit of the filing date of the parent application. In addition, the limitations of 'A method for treating an animal against a microbe-induced disease' of claims 1-3, 5, 9-11, 12, 13, 14, 16, 20, 21, 22, 41, 42, and 44 are not granted the benefit of priority under 35 U.S.C. 119(e) for 60/135,870, 60/154,582, 60/174,256, and 60/020,089, because the limitations of 'A method for treating an animal against a microbe-induced disease' are directed to subject matter not adequately disclosed under 35 USC 112, first paragraph, in these four provisional applications. Accordingly, the limitations of 'A method for treating an animal against a microbe-induced disease' of claims 1-3, 5, 9-11, 12, 13, 14, 16, 20, 21, 22, 41, 42, and 44 are only granted the effective filing date of 05/25/2000. Furthermore, the limitations of 'A method for protecting an animal against a microbe-induced disease' of claims 1-3, 5, 9-14, 16, 20, 21, and 22 are entitled only to the filing date of the continuation-in-part application, i.e. 07/09/2003, because the limitations of 'A method for protecting

an animal against a microbe-induced disease' are directed to subject matter not adequately disclosed under 35 USC 112, first paragraph, in either the parent applications, i.e. 09/996,420, 09/578,991, and 09/296,137, nor the PCT international application, i.e. PCT/US97/16,593. In addition, the limitations of 'Acinetobacter species; Brucella species; Bordetella species; Shigella species; Salmonella species; Klebsiella species; Enterobacter species; Pasteurella species; Streptobacillus species; Spirochetal species; Rhizobium species; Enterococcus faecalis; Enterococcus faecium; Acinetobacter baumanii; and Francisella tularensis' of claims 10, 11, 21, 22, and 42 are entitled only to the filing date of the continuation-in-part application, i.e. 07/09/2003, because these limitations are directed to subject matter not adequately disclosed under 35 USC 112, first paragraph, in either the parent applications, i.e. 09/996,420, 09/578,991, and 09/296,137, nor the PCT international application, i.e. PCT/US97/16,593. In a continuation-in-part application, only claims directed solely subject matter adequately disclosed under 35 USC 112, first paragraph in the parent application is entitled to the benefit of the filing date of the parent application.

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Withdrawn Objection/Rejection

In view of the new Oath-Declaration of inventor Irene Lee submitted on 4/5/2007 the defects in the oath/declaration has been corrected. Also, in view of the amendments to the specification reciting the status of each application, and amendments to the claims reciting the full name of "spp.", the objections are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5 and 9-11, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 "said microbe" lacks antecedent basis of support from the new limitation "bacterium".

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 1-3, 12-14, and 41, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Brasseur et al.

(Antimicrob. Agents Chemother., 411993, 37(4), pgs. 889-892) alone or as evidence by Barbas et al. (FEMS Microbiology Letters, 611990, 69(3) for reasons of record as reiterated below.

For claims 1, 12 and 41, Brasseur et al. disclose a curative therapy (refers to instant claimed method of treating) using sinefungin for immunosuppressed adult rats that are infected with *Cryptosporidium parvum* (refers to a microbe-induced disease) (see e.g. Abstract; pg. 889, left col., lines 15-20; pg. 890, left col., lines 9-22; pg. 890, right col., lines 3-26).

The methods comprise administering to the immunosuppressed adult rats that are infected with *Cryptosporidium parvum* a therapeutic effective dose of sinefungin (see e.g. pg. 890, left col., lines 9-22; pg. 890, right col., lines 3-26; pg. 889, Table 1; pg. 890, Tables 2 and 3; pg. 891, Table 4). Sinefungin is a known antibiotic wherein it inhibits the methyltransferase activity of parasites (see e.g. pg. 891, left col., lines 14-28).

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For claims 1-3, 13, and 14, although Brasseur et al. does not disclose that sinefungin inhibits the DNA adenine methyltransferase activity of parasites this property of sinefungin is well known in the art as evidenced by Barbas et al., pgs. 239-243 (see e.g. pg. 239, left col., lines 3-16; pg. 240, left col., lines 6-9; pg. 241, left col., line 31 thru right col., line 33). Therefore, the method of Brasseur et al. does anticipate the instant claimed invention.

Response to Arguments

Applicants state that Brasseur is concerned with the antiprotozoal activity (particularly, anti-Cryptosporidial activity) of sinefungin. The instant claims have been presently amended to provide methods of treating bacterium-related diseases.

In reply, attention is drawn at e.g., Summary section at page 239, col. 1:

Sinefungin is a naturally occurring nucleoside isolated from cultures of *Streptomyces griseolus* and *S. incarnatus*. It is structurally related to S-adenosyl-methionine (SAM) and S-adenosyl-L-homocysteine (SAH). Its effect and level of action on prokaryotes has not been studied with the same detail as with eukaryotic cells. ***In this report we describe the effect of sinefungin and SAH on several Streptomyces methyltransferases (DNA and protein MTases) and on other bacterial DNA-MTases.*** Protein MTases are resistant to sinefungin, whereas DNA-MTases are inhibited. Adenine

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MTases however, seem more sensitive to this analogue than cytosine Mtases.

Claims 1-3, 9-14, 20, 21, and 22, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Heithoff et al. (Science, 05/07/1999, 284(5416), pgs. 967-970).

Heithoff et al. disclose DNA adenine methylase (Dam-) mutants and methods of using the Dam- mutants (see e.g. Abstract; pg. 968, 1st col., line 5 thru 3rd col., line 27; pg. 969, 3rd col., lines 10-31). One method comprises the step of immunizing mice with a live attenuated vaccine (refers to instant claimed method step of administering of claim 12) containing Dam-mutants, which inhibit DNA adenine methylation (refers to instant claimed method step of inhibiting of claim 1) (see e.g. pg. 969, 3rd col., lines 10-31; pg. 969, Table 2). For claims 6, 9-11, 17, and 21-22, Heithoff et al. disclose that the vaccine protect the mice from Salmonella infection (refers to instant claimed microbe-induced disease) (see e.g. pg. 969, 3rd col., lines 10-31; pg. 969, Table 2). Therefore, the method of Heithoff et al. does anticipate the instant claimed invention

Response to Arguments

Applicants state that Heithoff is concerned with the prevention and/or treatment of microbial diseases. With respect

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to claims to treatment of bacterium-related diseases, the Applicants respectfully submit that the rejected claims are supported under 35 USC 112, 1st paragraph by the disclosure of PCT/US97/16593, from which priority is properly claimed under 35 USC 365(c). In support, the applicants note the disclosures therein in at the paragraph bridging pages 5 and 6, for example.

In reply, paragraph bridging pages 5 and 6 of the PCT/US97/16593 states:

Finally, this invention also provides therapeutic methods. These include methods of detecting infections with *Brucella* spp. and *H. pylori* by detecting the presence or absence of specific sequences of *Brucella* or *H. pylori* adenine methyltransferases or by detecting the proteins themselves using antibodies. **Other methods include treating conditions caused by *Agrobacterium* spp., *Rhizobium* spp, and *Helicobacter* spp.** Other methods involve administering to a mammal a therapeutically effective dose of a composition comprising a methyl transferase inhibitor and a pharmacological excipient. For animal associated bacteria, methods are preferably performed on mammals such as mice, rats, rabbits, sheep, goats, pigs, more preferably on primates including human patients.

That is the treatment method is drawn to the three recited species as recited above and Examples 2-4, as similarly relied upon by applicants.

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Claims 1-3, 5, 6, 9-14, 16, 17, 20, 21, 22, 41, 42, and 44 are rejected under 35 U.S.C.102(e) as being anticipated by Mahan et al. (US Patent 7,026,155 B2; effective filing date of 02/02/1999)

For claims 1-3, 12-14, and 41, Mahan et al. disclose a composition and methods of making and using the composition that renders the bacteria non-pathogenic (see e.g. Abstract; col. 1, lines 29-37; col. 10, lines 5-15; col. 10, lines 49-64). The methods include a method of treating an individual infected with a pathogenic bacteria (refers to instant claimed method of treating of claims 1, 2, and 41)(see e.g. col. 10, lines 49-52; col. 18, line 60 thru col. 19, line 5; col. 35, lines 19-34 and 44-67) and the method of using an immunogenic composition for eliciting an immune response in an individual against a pathogenic bacteria (refers to instant claimed method of protecting of claims 1 and 2)(see e.g. col. 10, lines 53-64; col. 35, lines 35-43). The method of treating comprises the step of administering to an individual a composition that alter the expression of or inhibit the activity of DNA adenine methylases (refers to instant claimed method step of inhibiting of claim 1; instant claimed method step of administering step of claims 12 and 41; and instant claims 2, 3, 13, and 14)(see e.g. col. 10, lines 49-52; col. 18, line 60 thru col. 19, line 5; col. 35,

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lines 19-34 and 44-67). The method of using an immunogenic composition for eliciting an immune response in an individual against pathogenic bacteria comprises the step of administering to an individual a composition that alter the expression of or inhibit the activity of DNA adenine methylases (refers to instant claimed method step of administering step of claims 1 and 12) (see e.g. col. 10, lines 53-64; col. 35, lines 35-43). The composition comprises a pharmaceutical acceptable excipient and an agent that alters the expression of or inhibits the activity of DNA adenine methylases (see e.g. col. 26, lines 27-46; col. 36, lines 19-48). For claims 5, 16 and 44, Mahan et al. disclose that the individual are human (see e.g. col. 19, lines 6-15) For claims 6, 9-11, 17, 20-22, and 42, Mahan et al. disclose that the pathogenic bacteria include Escherichia, Vibrio, Yersinia, Salmonella, and Helicobacter pylori (see e.g. col. 18, lines 32-38, col. 19, lines 35-47; col. 25, line 26 thru col. 26, line 26). Therefore, the methods of Mahan et al. do anticipate the instant claimed invention.

Response to Arguments

Applicants refer to their previous discussion of the priority properly claimed under 35 U.S.C 365(c) of

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PCT/US97/16593, and cite the same passages of the priority document.

In response, the reply above is also incorporated herein.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 4, 7-8, 15, 18-19, 23-40 and 43 drawn to non-elected invention. A complete reply to the

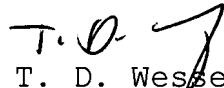
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final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
June 1, 2007